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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/590,451

08/24/2006

Mika Jokinen

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EXAMINER

YEAGER, RAYMOND P

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/590,451	Applicant(s) JOKINEN ET AL.	
	Examiner RAYMOND P. YEAGER	Art Unit 4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-37 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application 10/590,451 (08/24/2006) is a national stage entry of PCT/FI05/50046 (02/22/2005) per 35 USC 371 and claims foreign priority to Finland 20040312 (02/27/2004) per 35 USC 119. Claims 1 to 37 are pending.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1 to 19 are drawn to *a process of making a SiO₂ monolith, coating, or particle.*

Group II, claims 20 to 37 drawn to *a bioresorbable SiO₂ monolith, coating, or particle.*

Group III(a), claim 36 is drawn to *a process of using an SiO₂ monolith on humans and animals.*

Group III(b), claim 37 is drawn to *a process of using an SiO₂ monolith on plants.*

2. As set forth in Rule 13.1 of the Patent Cooperation Treaty (PCT), "the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept." Moreover, as stated in PCT rule

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13.2, "Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features." Furthermore, Rule 13.2 defines "special technical features" as "those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art"

3. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

The special technical feature of Group I is the *process of using an SiO₂ monolith*. The *process of using an SiO₂ monolith* of claim 1 does not present a contribution over the prior art. Claim 1 lacks an inventive step over WO1997/43567 (12/04/1997) (as disclosed in the IDS), hereafter referred to as the '367 publication, in view of Danilyuk, et al, 1998, Kortesus, 2001, iRao and Parvathy, 1993, Pope and MacKenzie, 1986, and Siouffi, 2003.

- Instant claim 1. "*A method for preparing a sol-gel derived SiO₂ monolith,*" - Kortesus, 2001 teaches the preparation of sol-gel processed monoliths and microparticles (page 20, section 4.20). The '367 publication discloses a process of preparing a silica-xerogel (page 7, lines 9 to 16). Danilyuk, et al, 1998 teaches a method of making SiO₂ monoliths (page 194, paragraph 4, to page 195, paragraph 1). Rao and Parvathy, 1993 teach the process of making a silica aerogel (page

3021-3022, sections 2.1 and 2.2). Siouffi, 2003 teaches the process of making silica based monoliths (page 804, section 3.1)/

- *“preferably with a minimum diameter of ≥ 0.5 mm, coating, preferably with a thickness of < 0.5 mm, or particle, preferably with a maximum diameter of $\leq 100 \mu\text{m}$,”* Danilyuk et al, 1998 teaches monoliths of about 20-40 mm (page 196, paragraph 3), and particles of 2 to 7 nm (page 196, paragraphs 3-5). As noted in the MPEP § 2144.05.I. “In the case where the claimed ranges ‘overlap or lie inside ranges disclosed by the prior art’ a prima facie case of obviousness exists. [*In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)]. Because the ranges in Danilyuk, et al, 1998 overlap with the ranges in the instant application, the ranges are anticipated per MPEP § 2144.05.I.
- *“with a very fast bioresorption rate,”* – The instant application discloses that bioresorption means “the degradation of materials in contact with a living organism, mostly for implanted biomaterials in living tissue.” The applicant claims alteration of the bioresorption rate but does not disclose a value or range for 'fast bioresorption'. The applicant merely discloses the use of “alkoxy-based sol-gel or inorganic silicate method that can be adjusted to be friendly for several kinds of biological active agents by adjusting the precursor ratios (water-to-alkoxide ratio, alcohol amount, pH), aging of the sol and by using different preparation methods.” The ‘367 publication teaches the silica-xerogel...dissolves controllably, and the release of the biologically active agent from the silica-

xerogel...is based on this dissolution, which allows consistent local release of the biologically active agent into the tissue. The release rate of the biologically active agent can be controlled via processing parameters of the gelation conditions.” Kortesu, 2001 address the effect of each parameter on the release rate of the drugs and degradation of the silica gel (page 8, table 2, page 31, section 6.1, and page 35, section 6.1.3) addressing particularly size, shape (page 25, section 5.1.1), pH, water/tetraethoxysilane ratio (pages 25-26, section 5.1.2 and page 32-33, section 6.1.1.1), alkyl-substituted gels (page 27, section 5.1.3 and page 33, section 6.1.1.2), and drug concentration (page 28, section 5.1.4 and page 34, section 6.1.2). Per MPEP § 2144.05.II “Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. ‘[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.’ *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)”. Thus it would be obvious to one of ordinary skill in the art to optimize these parameters for the best bioresorption. Siouffi, 2003 teaches the formation of a sol that is converted to a gel through polycondensation of the sol (page 804, section 3.1).

- “said SiO_2 optionally comprising a specific percentage or percentages of a biologically active agent or agents other than the SiO_2 itself with or without protective agent or agents for said biologically active agent or agents,” – The

instant application does not disclose 'specific percentages' and using the broadest reasonable interpretation, a 'specific percentage' could be 0 to 100 percent. Further, the language here in the instant application claims a monolith "with or without protective agents". The '367 claims a silica-xerogel with a biological agent (page 23, claim 7) and Danilyuk, et al, 1998 discloses a monolith without a biological agent (page 193, abstract), thus these two documents anticipate a monolith with or without a biological agent.

- *"wherein method a sol-gel derived SiO₂ is prepared from a sol comprising water, an alkoxide or inorganic silicate and a lower alcohol, i.e. an alcohol with 4 carbons, using a mineral acid or a base as a catalyst, preferably a mineral acid, and said sol is aged and dried characterised in that"* – The '367 publication prepares SiO₂ with a method comprising water, tetraethoxysilane (TEOS), ethanol, and nitric acid (examples 2 and 3). While the '367 publication does not explicitly teach the nitric acid is a catalyst, it is well known that nitric acid is a mineral acid and would have the same properties as the claimed mineral acid per MPEP § 2144.09: "A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. 'An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties.' [In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)]." In the '367 publication ,

nitric acid, a mineral acid, serves as the catalyst. Rao and Parvathy, 1993 teach adding water to TEOS in the presence of an acid or base catalyst (one example which is HCl, a mineral acid on page 3026, section 4) followed by addition of ethanol and aged (page 3021, section 2.1). Rao and Parvathy, 1993 also teach a supercritical drying step (page 3022, section 2.2). Rao and Parvathy, 1993 teach the optimization of catalyst effect, pH, ethanol/TEOS molar ratio, and ageing for best quality monolithicity and transparency. Siouffi, 2003 notes that many papers age the gel without indication of the procedure (page 808, column 2, paragraph 2).

- *“a) in the sol the starting”* – Siouffi, 2003 teaches a wide range of water/TEOS and alcohol/TEOS ratios (page 806, table 2).
- *“i) pH is from 0.05 to 2.5, preferably 1.5 to 2.5, most preferably 2.0,”*
 - Kortessuo, 2001 teaches the optimum release profile of dexmedetomidine is obtained from silica gels prepared at the isoelectric point for silica (pH = 2.3). Rao and Parvathy, 1993 teach the optimum pH is 2.0 to achieve the best monolithicity (page 3026, section 4). Pope and MacKenzie teach the effects of catalysts on pH and gelation rate of the silica gel (page 187, table 2).
- *“ii). molar ratio of water to the alkoxide or inorganic silicate is 0.5 to 2.5; preferably 1.5 to 2.5,”* – Siouffi, 2003 teaches a molar ratio of at least 2 to 1 is required to approach complete hydrolysis of the

alkoxide. Because Siouffi, 2003 anticipates the instant case per MPEP § 2144.05.I.

- “iii). molar ratio of alcohol to the alkoxide or inorganic silicate is ≥ 0.5 , preferably ≥ 1.0 ; and” – Rao and Parvathy, 1993 teach the optimization of the alcohol to alkoxide ratio by varying the ratio from 1 to 20. Per MPEP § 2144.05.II. it would be obvious to one of ordinary skill in the art to optimize the alcohol to alkoxide ratio.
- “b) either, i) the sol is, without induced changes of sol composition, let to gel spontaneously at a temperature of $\leq 25\text{ }^{\circ}\text{C}$ or an elevated temperature of $65\text{ }^{\circ}\text{C}$ to $90\text{ }^{\circ}\text{C}$, preferably at an elevated temperature of $65\text{ }^{\circ}\text{C}$ to $90\text{ }^{\circ}\text{C}$, or gelation of the sol is done by forced drying of the sol, or ii) a change or changes of sol composition are induced after sol ageing but before gel formation, said change or changes of sol composition optionally comprising addition of said biologically active agent or agents with or without said protective agent or agents, and the ratio t/t_{gel} is ≥ 0.005 , preferably ≥ 0.1 , most preferably ≥ 0.9 , wherein t is the ageing time of the sol, i.e. time from preparation of said sol to the induced changes, and t_{gel} is the time point where the sol would have turned to a gel without the induced changes; and forced drying of the sol is carried out or initiated within a time of ≤ 30 minutes, preferably ≤ 15 minutes, most preferably ≤ 5 minutes, from said induced change or

changes.” – The instant application claims the sol is dried without changes or changes occur prior to gelation such that the ageing time of the sol is accelerated 10 to 200 percent over the normal gelling time. Kortesus, 2001 teaches the addition of toremifene citrate prior to spray drying. Though no temperature is cited, a standard assumption is the process occurs at room temperature (<25°C). Rao and Parvathy, 1993 allowed gelation at ambient temperature (22-27°C).

- The ‘367 publication, Danilyuk, et al, 1998, Kortesus, 2001, Rao and Parvathy, 1993, and Siouffi, 2003 teach the behavior of xerogels is dependent on the parameters discussed *supra* and this would inherently alter degradation and in turn a release profile of a drug contained in the gel. The MPEP § 2112 notes: “The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. ‘The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness.’ [*In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995)].” Thus as discussed *supra* varying the pH parameter, molar ratios (water to alkoxide and/or alcohol to alkoxide), temperature of gelation, temperature of drying, process of drying, or ageing time is merely one of several normal control parameters well-known in the previous literature that a person of ordinary skill in the art would optimize without undue experimentation to make a sol-gel derived SiO₂ monolith, coating, or particle(s).

As disclosed in the '367 publication, Danilyuk, et al, 1998, Kortesus, 2001, Rao and Parvathy, 1993, Pope and MacKenzie, 1986, and Siouffi, 2003 the *process of making a SiO₂ monolith, coating, or particle* of instant claim I is not novel. The process in claim 1 can be used as a matrix for *in vitro* toxicity testing. As such, Group I does not share a special technical feature with the instant claims of Groups II-III. Therefore, the claims are not so linked with the meaning of PCT Rule 13.2 so as to form a single inventive concept, and unity between Groups I-II is broken.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

5. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to

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be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Election of Species

6. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

7. The applicant must elect the following species:

- If applicant elects Group I, II, III(a), or III(b), the following species elections are required:

- (A) One specific *embodiment of the sol-gel* (i.e. a monolith, coating, or particle);
- (B) The applicant must elect whether which step is present, either:
 - (1) “*The sol is, without induced changes of composition*” or
 - (a) “*Let to gel spontaneously at a temperature*” or

- If elected the applicant must elect *one temperature range*;
- (b) “*Gelation of the sol is done by forced drying*”;
- (2) “*A change or changes of sol composition are induced after sol ageing but before gel formation*”;
 - If this step is elected the applicant must elect:
 - (a) The *presence or absence* of the step comprising the addition of a biological active agent or protective agent; AND
 - (b) The presence or absence of forced drying and when it occurs in the process (30 minutes after, 15 minutes after, 5 minutes after, later)
 - (C) The applicant must elect if the *method of drying* is present or absent and if present the applicant must elect *one method of drying*.

Specifically, Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The applicant must elect the species as discussed *supra*. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Whether the applicant elects group I, II, III(a), or III(b), the applicant must elect one *embodiment of the sol-gel (A)*, one step from (B) (either B.1.a. (with one *temperature range*) or B.1.b. or B.2. or B.2.a or B.2.b), and if present one *method of drying (C)*, for prosecution on the merits to which the claims shall be restricted if no

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generic claim is finally held to be allowable. Currently, claim(s) 1 and 2 are generic for group I, and no claims are generic for groups II, III(a), III(b), IV(a), or IV(b).

8. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

9. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding technical feature as discussed *supra*.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are

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added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitation of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

10. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to RAYMOND P. YEAGER whose telephone number is

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(571)270-7681. The examiner can normally be reached on Mon - Fri 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

R.P.Y.

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4121